REMARKS

Applicants note with appreciation the Examiner's entry of the Applicants' Amendment of December 23, 2002. Claims 8, 32-35 and 37-38 remain under consideration. Claims 9 and 31 have been canceled.

Applicants note with appreciation the withdrawal of the objection to the Specification, Claims and Abstract in view of the Applicants' amendments. Applicants further note with appreciation the Examiner's withdrawal in part of the rejection of Claims 31-38 under 35 U.S.C. § 112, second paragraph and the withdrawal of the rejection of Claims 31-38 under 35 U.S.C. § 103(a).

Turning now to Examiner's request for submission of a new PTO-1449 form listing reference "FR 2772730", the Applicants submit herewith a copy of the PTO-1449 along with the Search Report for parent PCT/FR99/00404 which was filed in the U.S. Patent Office on September 5, 2000 with the original application showing the correct reference number FR 2744730 not FR2772730 as indicated in paragraph 6 of the aforementioned Official Action. Applicants further acknowledge and appreciate the Examiner's acknowledgement of papers submitted under 35 U.S.C. § 119(a)-(d).

The Applicants have amended the Specification and Brief Description of the Drawings in accordance with the Examiner's helpful suggestion.

Claim Rejections – 35 U.S.C. § 112, first paragraph

Claims 8, 9, 31-35 and 37-38 have been rejected under 35 U.S.C. § 112, first paragraph as lacking enablement.

Applicants respectfully submit that in light of the detail teachings of the Specification, which

disclose not only the nucleic and amino acid sequence for the TRAAK channel proteins, but also specific structural and functional components of the TRAAK channel proteins, the specification is fully enabled. Specifically, Applicants have illustrated unique electrophysiological properties of both the TREK-1 and TRAAK channels, and further illustrated that among the TWIK type K^+ channels, both the TREK-1 and TRAAK channels are, in fact, activated by a tension applied to the plasma membrane. (Page 16 of Applicants' Specification). Furthermore, TRAAK and TREK-1, which are both members of a TWIK-1 potassium channel family, have been identified as containing four transmembrane segments and two P domains. As a result, the structural and functional characteristics of both the TREK-1 and TRAAK-1 proteins have been clearly defined by the Applicants' Specification.

Applicants have characterized that the TRAAK protein is activated by polyunsaturated fatty acids, as well as the neuroprotective agent, riluzole.

In view of the detailed structural and functional characteristics of both the TRAAK and TREK-1 proteins, including activation by either riluzole or polyunsaturated fatty acids, the Applicants respectfully submit that one skilled in the art can easily practice the invention as recited in the solicited claims with little experimentation. The specification provides more than ample disclosure such that undue experimentation is just not necessary.

Applicants submit that "a functional equivalent derivative" is clearly described on page 6, lines 5-12, of the Applicants' Specification which states:

> Such derivatives include those with a sequence comprising a modification and/or a suppression and/or an addition of one or more amino acid residues, as long as this modification and/or suppression and/or addition does not modify the properties of the TRAAK channel. Such derivatives can be

> analyzed by the expert in the filed using the techniques described in the examples presented below which enable demonstration of the biophysical and pharmacological properties of the TRAAK channel.

One skilled in the art can simply use the Applicants' sequence to detect homologous sequences in public DNA data libraries, such as Genbank and EMBL employing techniques, such as the BLAST alignment program. Then, one skilled in the art can use the resulting cDNA to make a protein, and compare that protein to the structural and functional characteristics disclosed by the Applicants. Specifically, one skilled in the art can determine whether their newly isolated cDNA and its protein, contained four transmembrane segments, and two P domains. Next one skilled in the art can determine whether their protein is a leakage channel protein, and whether or not the newly found protein was activated by polyunsaturated fatty acids or riluzole to characterize whether it contained TRAAK's unique electrophysiological properties. This series of steps is not considered by those of ordinary skill in the art to be undue experimentation---only ordinary experimentation.

As an illustrative example, Applicants respectfully submit that the process described in the Specification, enabled the Applicants to isolate the TRAAK and TREK-1 proteins.

Applicants respectfully submit that the functionally equivalent derivatives do not need to be screened with all possible substances to determine whether or not the functionally equivalent derivatives attract channel proteins. Specifically, screening a functionally equivalent derivative can be done with polyunsaturated fatty acids or riluzole, which the Applicants has demonstrated reacts specifically to activate the TRAAK channel protein.

Turning now to the Examiner's suggestion that certain "regions can tolerate only relative conservative substitutions or no substitution," the Applicants respectfully submit the certain amino

acids substitutions are deemed conservative because in families of homologous proteins (e.g. potassium transport proteins) are found to occur more often than others. Specifically, certain conservative substitutions of one amino acid for another of like size hydrophobicity, charge, and R group is much more likely to be tolerated than a more radical substitution which will cause a non-functionally equivalent derivative. Consequently, the Applicants' claims are drawn to substitutions which are conservative, owing to the fact that function as a potassium transport protein namely, TRAAK type potassium channel transport must be retained. To limit the Applicants' claims to the specific sequence disclosed and described in the Specification, would fail to adequately protect the Applicants' invention. The Court of *In re Goffe,* which dealt with "suitable agglomerable particles" is applicable to the Application at bar. The Court stated that:

> To provide effective incentives, claims must adequately protect inventors.
>
> To demand that the first to disclose for limited claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process such as the one here and involved would not serve the constitutional purpose of promoting progress in the use thereof.

Applicants respectfully invite the Examiner's attention to 2164.06 of the MPEP, which states that "the quantity of experimentation needed to be performed by one skilled in the art is only **one** factor involved in determining whether undue experimentation is required to make and use the invention." *In re Colianni,* 195 USPQ 150 (CCPA 1977) **[emphasis added]**. The test for undue experimentation is not merely a quantitative measure since a considerable amount of experimentation is permissible if it is merely a routine, or if the Specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation is presumed. (*In re Wands,* 8 USPQ2d

1400, 1404 (Fed. Cir. 1998)). The Applicants also invite the Examiner's attention to the case of *In re Bundy*, wherein the court ruled that appellant's disclosure is sufficient for one skilled in the art to use claimed analogs of a naturally occurring prostaglandin, even though the specification lacked examples of specific analogs, because the specification had taught that the novel prostaglandin had certain pharmacological properties, which one skilled in the art could test for. *In re Bundy* 209 USPQ 48, 51-52 (CCPA 1991).

Much like the Applicants' disclosure which has expanded upon the knowledge of the known TWIK family of channel proteins, the Applicants have demonstrated that the novel TRAAK protein and the functionally equivalent derivatives thereof have a demonstrated and particular biophysical property which can be used to screen out non-functional derivative proteins of TRAAK. Applicants respectfully submit that the data in cloning libraries, and BLAST technologies, along with the specific structural and functional characteristics of TRAAK, allow one skilled in the art to find functionally equivalent derivatives of. Specifically, if a functionally equivalent derivative protein does not react with a polyunsaturated fatty acid or riluzole and/or lacks structural similarity to TRAAK (four transmembranal regions and two P domains), one skilled in the art would reasonably conclude that they were not in possession of a functionally equivalent derivative of a TRAAK protein.

Turning now to page 11 of the Office Action, which states that "conception is not achieved until reduction to practice has occurred", the Applicants respectfully submit that at the time the Application was filed, the claimed invention needs to be capable of being reduced to practice. Oregon Health and Science Univ. v. Vertex Pharm. Inc., 66 USPQ2d 1381 (D.C. Ore 2002). The

Applicants have described a specific method for isolating homologous cDNA, and the testing resulting protein of that cDNA to determine structural and functional proximity to TRAAK.

Turning to the rejection of Claim 33, the Applicants respectfully submit that the properly transformed host cell, which is cultured for expression in brain, cerebellum, spinal cord, and retinal neural tissues is fully enabled by the Specification. Specifically, the Examiner's attention is invited to page 14 and Fig. 3, of the Applicants' Specification wherein it is shown that TRAAK is exclusively expressed in the neural tissues, such as the brain, cerebellum, spinal cord and retina. Hence, given well-known culturing techniques, one skilled in the art would readily recognize how to culture the host cell and subsequently express it in neural tissues. Applicants respectfully submit that culturing the host cell for expression in tissue is a well understood practice. The Applicants are not claiming the use of a transgenic analog, rather they claim a method to transform a cellular host to contain a TRAAK potassium channel protein, and subsequently culture the host so that it may be expressed in neural tissues.

In view of the foregoing, Applicants respectfully submit that the amended claims are fully supported by the Specification.

35 U.S.C. § 112, second paragraph

Claims 8, 9, 31-35 and 37-38 have been rejected under 35 U.S.C. § 112, second paragraph. Applicants respectfully submit that as a result of the amendments these rejections are now obviated. Specifically, the Applicants have amended the acronym "TRAAK" to clearly spell out the term in all independent claims. Applicants have amended Claim 9 to remove reference to nucleotides 484

to 1576. Claims 8, 9, 31-35 and 37-38 have been amended to clearly relate back to the preamble, and further, the term "activity" has been amended to "potassium currents." Applicants have also amended the term "effect" in Claims 31-38 to "potassium currents" in accordance with the Examiner's helpful suggestion.

In view of the foregoing amendments and further rights of the remarks set forth above, the Applicants submit the Application is now in condition for allowance which action is respectfully requested.

Respectfully submitted,

T. Daniel Christenbury
Reg. No. 31,750

TDC:JEB:pam
(215) 656-3381